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FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY, DOCKET NO. SCIOS.012A	APPLICATION NO. 09/754,949	
	DISCLOSURE STATEMENT	APPLICANT METHODS FOR IDENTIFYING I	NHIBITORS OF NEURONAL DEGENERATION	
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			U.S. PATENT DOCUMENTS			
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1	4,816,567	03/28/89	Cabilly et al.	530	387	04/08/83
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EXAMINER INITIAL		OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)			
бC	2	Annaert et al., "Presenilins: molecular switches between proteolysis and signal transduction", TINS, Vol. 22, No. 10, pp. 439-443 (1999).			
oc	3	Ashkenazi et al., "Death Receptors: Signaling and Modulation", Science, Vol. 281, pp. 1305-1308 (28 August 1998).			
. not included	4	Barradas et al., "The downregulation of the pro-apoptotic protein Par-4 is critical for Ras-induced survival and tumor progression", EMBO J., Vol. 18, No. 22, pp. 6362-6369 (1999).			
oc	5	Baumeister et al., "Human presenilin-1, but not familial Alzheimer's disease (FAD) mutants, facilitate Caenorhabditis elegans Notch signalling independently of proteolytic processing," Genes & Function, Vol. 1, pp. 149-159 (1997).			
00	6	Beaucage et al., "Deoxynucleoside Phosphoramidites – A New Class of Key Intermediates for Deoxypolynucleotide Synthesis", <u>Tetrahedron Letters</u> , Vol. 22, No. 20, pp. 1859-1862 (1981).			

EXAMINER	Chungshot	DATE CONSIDERED	04/02/0	2	
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ATTY, DOCKET NO. SCIOS.0124

APPLICATION NO. 09/754,949

INFORMATION DISCLOSURE STATEMENT

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APPLICANT
METHODS FOR IDENTIFYING INHIBITORS OF NEURONAL DEGENERATION

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EXAMINER INITIAL		OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
1	7	Beg et al., "An Essential Role for NF-κB in Preventing TNF-α-Induced Cell Death", Science, Vol. 274, pp. 782-784 (1 November 1996).
	8	Behl et al., "Glucocorticoids Enhance Oxidative Stress-Induced Cell Death in Hippocampal Neurons in Vitro", Endocrinology, Vol. 138, No. 1, pp. 101-106 (1997).
	9	Berra et al., "Positioning Atypical Protein Kinase C Isoforms in the UV-Induced Apoptotic Signaling Cascade", Mol. Cell. Biol., Vol. 17, No. 8, pp. 4346-4354 (1997).
	10	Boussif et al., "A versatile vector for gene and oligonucleotide transfer into cells in culture and in vivo: Polyethylenimine", Proc. Natl. Acad. Sci. USA, Vol. 92, pp. 7297-7301 (August 1995).
	11	Chui et al., "Transgenic mice with Alzheimer presenilin 1 mutations show accelerated neurodegeneration without amyloid plaque formation", Nature Med., Vol. 5, No. 5, pp. 560-564 (May 1999).
	12	Deng et al., "Alzheimer-associated presenilin-2 confers increased sensitivity to apoptosis in PC12 cells", FEBS Letters, Vol. 397, pp. 50-54 (1996).
	13	DeStrooper et al., "A presenilin-1-dependent γ-secretase-like protease mediates release of Notch intracellular domain", Nature, Vol. 398, pp. 518-522 (8 April 1999).
	14	Devin et al., "The Distinct Roles of TRAF2 and RIP in IKK Activation by TNF-R1: TRAF2 Recruits IKK to TNF-R1 While RIP Mediates IKK Activation", Immunity, Vol. 12, pp. 419-429 (April 2000).
	15	Diaz-Meco et al., "ζPKC induces phosphorylation and inactivation of lκB-α in vitro", EMBO J., Vol. 13, No. 12, pp. 2842-2848 (1994).
	16	Diaz-Meco et al., "Lambda-Interacting Protein, a Novel Protein That Specifically Interacts with the Zinc Finger Domain of the Atypical Protein Kinase C Isotype λ/ι and Stimulates its Kinase Activity In Vitro and In Vivo", Mol. Cell. Biol., Vol. 16, No. 1, pp. 105-114 (1996).
00	17	Diaz-Meco et al., "Inactivation of the Inhibitory κB Protein Kinase/Nuclear Factor κB Pathway by Par-4 Expression Potentiates Tumor Necrosis Factor α-induced Apoptosis", J. Biol. Chem., Vol. 274, No. 28, pp. 19606-19612 (July 1999).
	18	Diaz-Meco et al., "The Product of par-4, a Gene Induced during Apoptosis, Interacts Selectively with the Atypical Isoforms of Protein Kinase C*, Cell, Vol. 86, pp. 777-786 (1996).
	19	Fiers et al., "Complete nucleotide sequence of SV40 DNA", Nature, Vol. 273, p. 113-120 (May 11, 1978).
1	20	Frengen et al., "A Modular, Positive Selection Bacterial Artificial Chromosome Vector with Multiple Cloning Sites", Genomics, Vol. 58, pp. 250-253 (1999).
	21	"Methods in Enzymology," Vol. 185, Gene Expression Technology, Goeddel, D.V. Ed. (1990).
	22	Graham et al., "Characteristics of a Human Cell Line Transformed by DNA from Human Adenovirus Type 5", J. Gen. Virol., Vol. 36, pp. 59-72 (1977).
	23	Guo et al., "Increased vulnerability of hippocampal neurons to excitotoxic necrosis in presenilin-1 mutant knock-in mice", Nature Med., Vol. 5, No. 1, pp. 101-106 (January 1999).
	24	Guo et al., "Alzheimer's Presenilin Mutation Sensitizes Neural Cells to Apoptosis Induced by Trophic Factor Withdrawal and Amyloid β-Peptide: Involvement of Calcium and Oxyradicals", J. Neurosci., Vol. 17, No. 11, pp. 4212-4222 (June 1, 1997).
	25	Guo et al., "Par-4 is a mediator of neuronal degeneration associated with the pathogenesis of Alzheimer disease", Nature Med., Vol. 4, No. 8, pp. 957-962 (August 1998).
	26	Guo et al., "Alzheimer's PS-1 mutation perturbs calcium homeostasis and sensitizes PC12 cells to death induced by amyloid β-peptide", NeuroReport, Vol. 8, No. 1, pp. 379-383 (20 December 1996).
	27	Haass, "Presenilins: Genes for Life and Death", Neuron, Vol. 18, pp. 687-690 (1997).
	28	Heck et al., "Insulin-like Growth Factor-1-mediated Neuroprotection against Oxidative Stress is Associated with Activation of Nuclear Factor κΒ", <u>J. Biol.</u> Chem., Vol. 274, No. 14, pp. 9828-9835 (April 2, 1999).
	29	Herreman et al., "Presenilin 2 deficiency causes a mild pulmonary phenotype and no changes in amyloid precursor protein processing but enhances the embryonic lethal phenotype of presenilin 1 deficiency," Proc. Natl. Acad. Sci. USA, Vol. 96, No. 21, pp. 11872-11877 (October 12, 1999).
	30	Hsu et al., "TNF-Dependent Recruitment of the Protein Kinase RIP to the TNF Receptor-1 Signaling Complex", Immunity, Vol. 4, pp. 387-396 (April 1996).
	31	Ito et al., "Solid phase synthesis of polynucleotides. VI. Further studies on polystyrene copolymers for the solid support", Nucleic Acids Res., Vol. 10, No. 5, pp. 1755-1769 (1982).
	32	Jones et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse", Nature, Vol. 321, pp. 522-525 (29 May 1986).

EXAMINER WINDS AND

DATE CONSIDERED

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FORM PTO-1449

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EXAMINER INITIAL		OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
	33	Kaltschmidt et al., "Brain synapses contain inducible forms of the transcription factor NF-κΒ", Mech. Dev., Vol. 43, pp. 135-147 (1993).
	34	Kaltschmidt et al., "Inhibition of NF-κB potentiates amyloid β-mediated neuronal apoptosis", Proc. Natl. Acad. Sci. USA, Vol. 96, pp. 9409-9414 (August 1999).
	35	Kelliher et al., "The Death Domain Kinase RIP Mediates the TNF-Induced NF-κB Signal", Immunity, Vol. 8, pp. 297-303 (March 1998).
	36	Lallena et al., "Activation of IκB Kinase β by Protein Kinase C Isoforms", Molecular and Cellular Biology, Vol. 19, No. 3, pp. 2180-2188 (March 1999).
	37	Lassam et al., "Synthesis of DNA, Late Polypeptides, and Infectious Virus by Host-Range Mutants of Adenovirus 5 in Nonpermissive Cells," Virology, Vol. 87, p. 463-467 (1978).
	38	Lezoualc'h et al., "High Constitutive NF-κB Activity Mediates Resistance to Oxidative Stress in Neuronal Cells", The Journal of Neuroscience, Vol. 18, No. 9, pp. 3224-3232 (May 1, 1998).
	39	Levitan et al., "Facilitation of lin-12-mediated signalling by sel-12, a Caenorhabditis elegans S182 Alzheimer's disease gene", Nature, Vol. 377, pp. 351-354 (September 1995).
	40	Levy-Lahad et al., "Candidate Gene for the Chromosome 1 Familial Alzheimer's Disease Locus", Science, Vol. 269, pp. 973-977 (18 August 1995).
1	41	Li et al., "A Role for 12-lipoxygenase in Nerve Cell Death Caused by Glutathione Depletion", Neuron, Vol. 19, pp. 453-463 (August 1997).
	42	Liu et al., "Dissection of TNF Receptor 1 Effector Functions: JNK Activation is Not Linked to Apoptosis While NF-kB Activation Prevents Cell Death", Cell, Vol. 87, pp. 565-576 (1996).
70	43	MacDonald et al., "NGF-Resistant PC12 Cell Death Induced by Arachidonic Acid is Accompanied by a Decrease of Active PKC Zeta and Nuclear Factor Kappa B", Journal of Neuroscience Research, Vol. 57, pp. 219-226 (1999).
,	44	March, Advanced Organic Chemistry: Reactions, Mechanisms and Structure, 4th Ed., John Wiley & Sons, New York, NY (1992).
	45	Matteucci et al., "Synthesis of Deoxyoligonucleotides on a Polymer Support ¹ ", <u>J. Amer. Chem. Soc.</u> , Vol. 103, p. 3185-3191 (1981).
	46	Matteucci et al., "The Synthesis of Oligodeoxypyrimidines on a Polymer Support", Tetrahedron Letters, Vol. 21, pp. 719-722 (1980).
	47	McCarthy et al., "RIP2 is a Novel NF-kB-activating and Cell Death-inducing Kinase", The Journal of Biological Chemistry, Vol. 273, No. 27, pp. 16968-16975 (1998).
	48	Morrison et al., "Chimeric human antibody molecules: Mouse antigen-binding domains with human constant region domains", <u>Proc. Natl. Acad. Sci. USA,</u> Vol. 81, pp. 6851-6855 (November 1984).
	49	Murayama et al., "Direct association of presenilin-1 with β-catenin", <u>FEBS Letters</u> , Vol. 433, pp. 73-77 (1998).
	50	Ninomiya-Tsuji et al., "The kinase TAK1 can activate the NIK-IkB as well as the MAP kinase cascade in the IL-1 signalling pathway", Nature, Vol. 398, pp. 252-256 (18 March 1999).
	51	Nishimura et al., "Presenilin mutations associated with Alzheimer disease cause defective intracellular trafficking of β-catenin, a component of the presenilin protein complex", Nature Medicine, Vol. 5, No. 2, pp. 164-169 (February 1999).
	52	Ozes et al., "NF-kB activation by tumour necrosis factor requires the Akt serine-threonine kinase", Nature, Vol. 401, pp. 82-85 (2 September 1999).
	53	Pomerantz et al., "NF-kB activation by a signaling complex containing TRAF2, TANK and TBK1, a novel IKK-related kinase", The EMBO Journal, Vol. 18, No. 23, pp. 6694-6704 (1999).
	54	Quon et al., "Formation of β-amyloid protein deposits in brains of transgenic mice", Nature, Vol. 352, pp. 239-241 (18 July 1991).
	55	Riechmann et al., "Reshaping human antibodies for therapy", Nature, Vol. 332, pp. 323-329 (24 March 1988).
	56	Remington's Phamaceutical Sciences, 18 th Edition, Mack Publishing Co., Easton, PA (1990).
	57	Rogaev et al., "Familial Alzheimer's disease in kindreds with missense mutations in a gene on chromosome 1 related to the Alzheimer's disease type 3 gene", Nature, Vol. 376, pp. 775-778 (31 August 1995).
	58	Roperch et al., "Inhibition of presenilin 1 expression is promoted by p53 and p21WAF-1 and results in apoptosis and tumor suppression", Nature Medicine, Vol. 4, No. 7, pp. 835-838 (July 1998).
	59	Sambrook et al., Sections 16.32-16.37, Molecular Cloning: A Laboratory Manual, New York, Cold Spring Harbor Laboratory Press (1989).

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DATE CONSIDERED

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*EXAMINER: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.



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EXAMINER INITIAL		OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
1	60	Sanz et al., "The interaction of p62 with RIP links the atypical PKCs to NF-kB activation", The EMBO Journal, Vol. 18, No. 11, pp. 3044-3053 (1999).
	61	Saura et al., "Evidence that Intramolecular Associations between Presenilin Domains are Obligatory for Endoproteolytic Processing", The Journal of Biological Chemistry, Vol. 274, No. 20, pp. 13818-13823 (May 14, 1999).
	62	Sherrington et al., "Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease", Nature, Vol. 375, pp. 754-760 (29 June 1995).
· /	63	Singleton et al., Dictionary of Microbiology and Molecular Biology, 2 nd ed., J. Wiley & Sons, New York, NY (1978 & 1987).
	64	Song et al., "Proteolytic release and nuclear translocation of Notch-1 are induced by presentiin-1 and impaired by pathogenic presentiin-1 mutations", Proc. Natl. Acad. Sci. USA, Vol. 96, pp. 6959-6963 (June 1999).
	65	Taglialatela et al., "Inhibition of Nuclear Factor Kappa B (NFkB) Activity Induces Nerve Growth Factor-Resistant Apoptosis in PC12 Cells", <u>Journal of Neuroscience Research</u> , Vol. 47, pp. 155-162 (1997).
	66	Takashima et al., "Presenilin 1 associates with glycogen synthase kinase-3β and its substrate tau", Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 9637-9641 (1998).
	67	Thinakaran et al., "Evidence that Levels of Presenilins (PS1 and PS2) are Coordinately Regulated by Competition for Limiting Cellular Factors." The Journal of Biological Chemistry, Vol. 272, No. 45, pp. 28415-28422 (November 7, 1997).
01/	68	Thinakaran, "The role of presentiins in Alzheimer's disease", The Journal of Clinical Investigation, Vol. 104, No. 10, pp. 1321-1327 (November 1999).
1	69	Thinakaran et al., "Endoproteolysis of Presenilin 1 and Accumulation of Processed Derivatives In Vivo", Neuron, Vol. 17, pp. 181-190 (July 1996).
	70	Tomita et al., "C Terminus of Presenilin is Required for Overproduction of Amyloidogenic Aβ42 through Stabilization and Endoproteolysis of Presenilin", The Journal of Neuroscience, Vol. 19, No. 24, pp. 10627-10634 (December 15, 1999).
	71	Urlaub et al., "Isolation of Chinese hamster cell mutants deficient in dihydrofolate reductase activity", Proc. Natl. Acad. Sci. USA, Vol. 77, No. 7, pp. 4216-4220 (July 1980).
	72	Van Antwerp et al., "Suppression of TNF-α-Induced Apoptosis by NF-κΒ", Science, Vol. 274, pp. 787-789 (1 November 1996).
	73	Wang et al., "TNF- and Cancer Therapy-Induced Apoptosis: Potentiation by Inhibition of NF-κΒ", Science, Vol. 274, pp. 784-787 (1 November 1996).
	74	Wang et al., "Parenteral Formulations of Proteins and Peptides: Stability and Stabilizers," <u>Journal of Parenternal Science and Technology</u> , Technical Report No. 10, Supp. 42-2S (1988).
	75	Warzocha et al., "Antisense Strategy: Biological Utility and Prospects in the Treatment of Hematological Malignancies", Leukemia and Lymphoma, Vol. 24, pp. 267-281 (1997).
	<u> </u>	Wolozin et al., "Participation of Presenilin 2 in Apoptosis: Enhanced Basal Activity Conferred by an Alzheimer Mutation", Science, Vol. 274, pp. 1710-1713 (6 December 1996).
		Wooten et al., "Function for NF-kB in Neuronal Survival: Regulation by Atypical Protein Kinase C", <u>Journal of Neuroscience Research</u> , Vol. 58, pp. 607-611 (1999).
	78	Wooten et al., "Mapping of Atypical Protein Kinase C within the Nerve Growth Factor Signaling Cascade: Relationship to Differentiation and Survival of PC12 Cells", Molecular and Cellular Biology, Vol. 20, No. 13, pp. 4494–4504 (July 2000).
	79	Wu et al., "Inhibition of NF-κB/Rel induces apoptosis of murine B cells", The EMBO Journal, Vol. 15, No. 17, pp. 4682-4690 (1996).
		Yu et al., "The Presenilin 1 Protein is a Component of a High Molecular Weight Intracellular Complex that Contains β-Catenin", The Journal of Biological Chemistry, Vol. 273, No. 26, pp. 16470-16475 (1998).
	<u> </u>	Zapata et al., "Engineering linear F(ab´) 2 fragments for efficient production in Escherichia coli and enhanced antiproliferative activity, Protein Engineering, Vol. 8, No. 10, pp. 1057-1062 (1995).
	82	Zhang et al., "Destablization of β-catenin by mutations in presentiin-1 potentiates neuronal apoptosis", Nature, Vol. 395, pp. 698-702 (15 October 1998).

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